This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 215.

See attached form for Additional information.

FORM APPROVED
OMB NO. 0579-0036

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1.Certificate Number:74-R-0081
Customer Number: 1502

FORM APPROVED
OMB NO.0579-0036

ANNUAL REPORT OF RESEARCH FACILITY

University of North Texas Health Science Center
3500 Camp Bowie Blvd.
Fort Worth, Texas 76107
Telephone: (817) 735-2017

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS (Sites) - See Attached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (Attach additional sheets if necessary or use APHIS Form 7023A)

A. Animals Covered By the animal Welfare Regulations	B. Number of animal being b☐ red, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposed	C. Number of animals upon which teaching, Research, experiments Or test were conducted Involving no pain, Distress, or use of pain-Relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs was used.	E. Number animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilization drugs would have adversely affected the procedures, research or interpretation of the teaching, research, experiments, surgery, or tests. (An	TOTAL # OF ANIMALS COLUMN (C+D+E)
4. Dogs	2	0	44	0	44
5. Cats	0	0	0	0	0
6. Guinea Pigs	0	0	0	0	0
7. Hamsters	24	0	0	540	540
8. Rabbits	0	0	32	0	32
9. Primates	0	0	0	0	0
10. Sheep	0	0	0	0	0
11. Pigs	0	0	55	0	55
12.Other Farm Animals					
13. Goats	0	0	22	0	22
14. Other Animals					

ASSURANCE STATEMENTS

1. Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research teaching, testing surgery, or experimentation were followed by this research facility.

2. Each principal investigator has considered alternatives to painful procedures.

3. This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional animal Care and Use Committee (IACUC). A summary of all such exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4. The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal car and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
e Officer or Legally Responsible Institutional Official)

(b)(6), (6)(7)(C)	(b)(6), (6)(7)(C)	Date Signed 2008

Aphis form 7023 (Replaces VS FORM 18-23 (Oct 88), which is obsolete.

DEC 16 2008 ✓

DESCRIPTION

Explanation of Category E Animal

Protocol # 2006/07-06 "Experimental *Clostridium difficile* Infection in Hamsters"

Antibiotics are prescribed drugs used to combat bacterial infections in humans and animals. Because several bacteria have become resistant (can not be kidded) to many commonly used antibiotics, the discovery of new and improved antibiotics could be used to effectively treat resistant bacterial infections. The purpose of this project is to focus on the preclinical (before human) development and testing of new (test) antibiotics that can effectively treat intestinal infections caused by the bacterium, *Clostridium difficile.* This protocol will examine the effectiveness of antibiotic treatment in a hamster intestinal infection model with *C. difficile.* Ironically, antibiotic treatment for other bacterial infections often leads to *C. difficile* infections in humans. Clindamycin is an antibiotic frequently associated with *C. difficile* intestinal infections and will be used in this model to subcutaneously (beneath the skin) treat hamsters 24 to 48 hours prior to infection. Clindamycin treated hamsters will be orally infected with *C. difficile,* and oral treatment with a test antibiotic will be initiated 6 to 24 hours after infection. The test antibiotic can be given up to 3 times per day for up to 7 days of total treatment. Each study will incorporate up to 4 treatment groups (10 animals per group) and one control group (10 animals per group) for the duration of the study. At the end of a study, animals will be euthanized and sections of their intestines (cecum) will be removed. Antibiotic effectiveness (how well it works) in this model will be determined by the amount of bacteria recovered from the large intestine (cecum) of treated/infected animals after approximately 10 days. Also, to determine if the infection has spread to the blood, whole blood from treated/infected animals will be processed for bacterial recovery. Infected animals will be monitored daily for signs of an advanced disease state, which includes prolonged weight loss, an enlarged gut, and slow movement. If an animal exhibits these signs, animal facilities personnel will be notified and the animal will be euthanized. This model is critical in determining an antibiotic's utility in treating this type of infection.

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JUSTIFICATION

Explanation of Category E Animal

Protocol # 2006/07-06 "Experimental *Clostridium difficile* Infection in Hamsters"

The objective of this study is the pre-clinical evaluation of novel antibiotic classes in an intestinal infection model. Medicine used to relieve pain may interfere with the potential therapeutic effects a novel antibiotic may have in this model. Therefore, it is imperative that animals used in this model will be given pain relief in order to correctly assess the effectiveness of a test antibiotic.

The references are as follows:

- Anton, P.M., O'Brien, M., Kokkotou, E., Eisenstein, B., Michaelis, A., Rothstein, D., Paraschos, S., Kelly, C. P., Pothoulakis, C. (2004). Rifalazil Treats and Prevents Relapse of Clostridium difficile- Associated Diarrhea in Hamsters. *Antimicrop. Agents Chemother. 48: 3975-3979*
- Bailey, J.M., Erramousepe, J. (2004). Nitazoxanide Treatment for Giardiasis and Crypotosporidiosis in Childre. *Ann Pharmacother* 38: 634-640
- Guttner, Y.., Windsor, H.M., Viiala, C. H., Dusci, L., Marshall, B. J. (2003). -itazoxanide in Treatment of Helicobacter pylori: a Clinical and In Vitro Study. *Antimocrob. Agents Chemother.* 47: 3780-3783
- Stettler, M., Fink, R., Walker, M., Gottstein, B., Geary, T. G., Rossignol, J. F., Hemphill, A. (2003). In Vitro Parasiticadal Effect of Nitazoxanide against Echinococcus multilocularis Metacestodes. Antimocrob. Agents *Chemother.* 47: 467-474
- Sisson, G., Goodwin, A., Raudonikiene, A., Hughes, N.J., Mukhopadhyay, A. K., Berg, D. E., Hoffman, P.S. (2002). Enzymes Associated with Reductive Activation and Action of Nitazoxanide, Nitrofurans, and Metronidazole in Helicobacter pylori. *Antimicrob. Agents Chemother.* 46:2116-212
- Pelaez, T., Alonso, R., Perez, C., Alcala., L., Cuevas, O., Bouza, E. (2002). In Vitro Activity of Linezolid against Clostridium difficile. *Antimicrob. Agents Chemother.* 46:1617-1618

INTERVENTION

Animals are observed two-three times a day for the duration of the experiment for mortality and morbidity and for the presence of diarrhea. Criteria used to assign a moribund state are extended periods (6 days) of weight loss, progression to an emaciated state, prolonged lethargy (more than 3 days), signs of paralysis, skin erosions or trauma, hunched posture, and a distended abdomen. These moribund state effects can be a result of the infection and/or test antibiotic treatment. If a moribund state is detected for an animal, animal facilities personnel will be notified and a course of action (euthanasia) will be determined at that time.

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